Implications of Mycobacteria
in Clinical Disorders

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Avian mycobacteriosis is generally a disease of captive populations. In the past, most cases were believed to have been caused by *Mycobacterium avium* and *M. intracellulare*. More recently, however, the atypical organism, *M. genavense*, has emerged as a significant cause of disease. Although the incidence of disease is relatively rare, the potential for avian mycobacteriosis to spread to humans makes this subject pertinent for avian veterinarians. In this chapter, aspects of avian mycobacteriosis, including clinical presentation, therapeutic options, zoonotic potential and diagnostic tests with promising new molecular techniques such as deoxyribonucleic acid (DNA) probes, will be covered.

Mycobacterium spp.

Mycobacterium avium and *M. intracellulare* are frequently grouped together as the *Mycobacterium avium intracellulare* (MAI) complex or *Mycobacterium avium* complex (MAC). Twenty-eight seeknown serotypes of MAI exist.[56] The more pathogenic serotypes 1, 2 and 3 belong to the *M. avium* group.[20,54] Serotypes 4 to 28 make up the *M. intracellulare* group, which is considered relatively avirulent.[31,56,77] Historically, these two species were considered the cause of avian tuberculosis, and they still play an important role in avian mycobacteriosis today.

The atypical organism, *Mycobacterium genavense*, is an important cause of mycobacteriosis, especially in companion birds.[38,40-42] In a recent survey of necropsied pet birds in Europe, *M. genavense* was the predominant mycobacterial species isolated.[49] *Mycobacterium genavense* is a fastidious organism only recently identified. It is most closely related to *M. simiae* and was first isolated from immunosuppressed human patients.[10,19,84] Addi-

tional atypical mycobacteria isolated from companion birds in rare instances include *M. fortuitum*, *M. gordonae* and *M. nonchromogenicum*.[38,41,70,79]

There also are rare reports of disease caused by *Mycobacterium tuberculosis* or *M. bovis*.[80] All avian species studied have been relatively resistant to *M. bovis*.[13] *Mycobacterium tuberculosis* has been reported only in companion parrot species.[29,36,77,80] There are no case reports, as yet, of *M. tuberculosis* in passerines or free-ranging psittacines.[13,48] Infection is probably secondary to close contact with infected humans.[31,48] *Mycobacterium tuberculosis* was cultured from a green-winged macaw (*Ara chloroptera*) 3 to 4 years after active tuberculosis was diagnosed in two human occupants of the household.[85]

Pathogenesis of Disease

SOURCE OF INFECTION

Mycobacterium is a ubiquitous environmental saprophyte most commonly found in soil with heavy fecal contamination or other organic debris.[31] High levels of mycobacteria also might be found in surface water or in marshy, shaded areas.[20,77] Although wild birds are a possible source of infection, they are probably not an important source of disease for captive birds.[6,18,43,77] The prevalence of mycobacteriosis is low (usually <1%) in most free-ranging populations.[24]

TRANSMISSION

Avian mycobacteriosis is usually transmitted by the ingestion or inhalation of soil or water contaminated by feces, or, less commonly, by urine.[29,82] Raptors might become infected by ingesting infected prey. A mechanical arthropod vector is a rare mode of transmission. Vertical transmission also is possible, however, avian mycobacteriosis is generally associated with an immediate halt in reproductive activity.[77]

Pathogenesis

The primary site of entry and initial colonization of mycobacteria is the intestine. Subclinical bacteremia quickly follows and the organism spreads to the liver through the portal circulation. The absence of lymph nodes in the bird then allows mycobacteria to spread hematogenously to distant parenchyma such as the spleen, bone marrow, skin and lungs.[29,36,80]

Disturbance of contaminated surface water might lead to the inhalation of aerosolized mycobacteria and direct colonization of the respiratory tract. Focal skin disease probably occurs secondary to the inoculation of *Mycobacterium* spp. into mucosal or dermal lesions, or by the use of contaminated needles.[36,83]

HOST IMMUNE RESPONSE

The presence of humeral antibodies does not appear to protect against the development of avian mycobacteriosis.[20,82] In the mammal, cell-mediated immunity is much more important, and this also may be true in the bird. Studies evaluating growing layer hens inoculated with *Mycobacterium butyricum* found that dietary linoleic acid may boost cell-mediated immunity.[69]

Clinical Disease

INCIDENCE

The distribution of avian mycobacteriosis is worldwide, although most reports of disease are from northern hemisphere's temperate zones. The incidence of avian mycobacteriosis is reportedly uncommon in some countries, such as Japan.[49,68]

SIGNALMENT

Adult birds, 3 to 10 years of age, are most frequently diagnosed with avian mycobacteriosis.[20,51,80] There is probably no gender predilection, although some reports suggest a slightly higher incidence of disease in the female bird.[42,77,80]

Avian mycobacteriosis has been reported in virtually all avian taxonomic orders, however, susceptibility varies **(Table 28.1)**. The greatest incidence of disease has been in captive collections of waterfowl, parrots, songbirds, and ground-dwelling birds such as farmed ratites and small poultry flocks. Reports also are common in the wood pigeon (*Columba palumbus*) and free-ranging waterfowl. Orders Falconiformes and Gruiformes also are considered susceptible.[6,16,20,24,27,41,43,44,49,59,60,77,80]

Species considered relatively resistant to avian mycobacteriosis include rooks (*Corvus frugilegus*), turtle doves (*Streptopelia risoria*), turkey (*Meleagridis* spp.) and guinea fowl (*Numida meleagris*). Although the flamingo formerly was considered fairly resistant to avian mycobacteriosis, an epidemic was reported in lesser flamingos (*Phoeniconaias minor*) in 1993. More than 18,500 birds died over a 3-month period.[45,77]

CLINICAL PICTURE

There are three forms of avian mycobacteriosis, which have been historically described as classical, paratuberculous or diffuse disease. The most common form of disease in the avian patient involves granulomatous lesions

Table 28.1 | Species Highly Susceptible to Avian Mycobacteriosis[1,6,12,16,17,22,24,27,29,39,41,43,44,46,49,59,60,62,75,77,80,86,87,88]

Order	Species
Anseriformes	• White-winged wood duck (*Aix sponsa*) • Sea ducks (*Somateria fischeri, Clangula hyemalis, Melanitta* spp.)
Columbiformes	• Wood pigeon (*Columba palumbus*)
Falconiformes	
Galliformes	• Partridge (*Alectoris* spp., *Lerwa* sp., *Ammoperdix* spp., *Tetraogallus* spp.) • Pheasants (*Phasianus colchicus*) • Quail (*Coturnix japonica*)
Gruiformes	• Cranes (*Grus* spp., *Balearica* spp., *Anthropoides* spp.) • Rails (*Rallus* spp., *Laterallus jamaicensis*) • Gallinules (*Porphyrula* spp.) • Coots (*Fulica* spp.)
Passeriformes	• Canaries (*Serinus canarius*) • Sparrows (*Passer domesticus*) • Hooded siskin (*Spinus* sp.) • Lady Gouldian (*Chloebia gouldiae*)
Psittaciformes	• Amazon parrots (*Amazona* spp.) *Amazona ochrocephala auropalliata, Amazona farinosa, Amazona aestiva* • Grey-cheeked parakeet (*Brotogeris pyrrhopterus*) • Budgerigar (*Melopsittacus undulatus*) • Horned parakeets (*Eunymphicus cornutus*) • Pionus (*Pionus* sp.) • Ring-necked parakeets (*Psittacula*)

Table 28.2 | Incidence of Granulomatous Lesions with Avian Mycobacteriosis[29]

	Common	Usually Absent
Charadriiformes (gulls, shorebirds)	✓	
Ciconiiformes (bitterns, herons, egrets, ibises)	✓	
Cuculiformes (cuckoos)	✓	
Falconiformes (hawks, eagles, falcons)	✓	
Galliformes (fowl)	✓	
Gruiformes (coots, cranes, rails)	✓	
Piciformes (toucans)	✓	
Strigiformes (owls)	✓	
Anseriformes (waterfowl)		✓
Columbiformes (pigeons, doves)		✓
Coraciiformes (hornbills, kingfishers)		✓
Passeriformes (songbirds)		✓
Psittaciformes (parrots)		✓
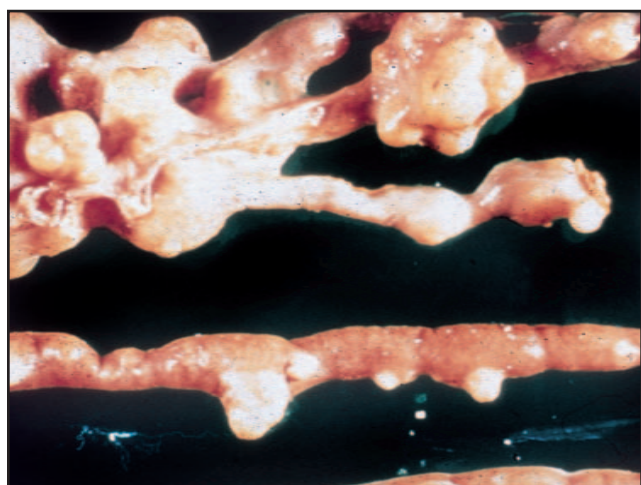
Fig 28.1 | Granulomatous intestinal lesions in a mallard duck (*Anas platyrhynchos*) caused by *Mycobacterium avium intracellulare*.
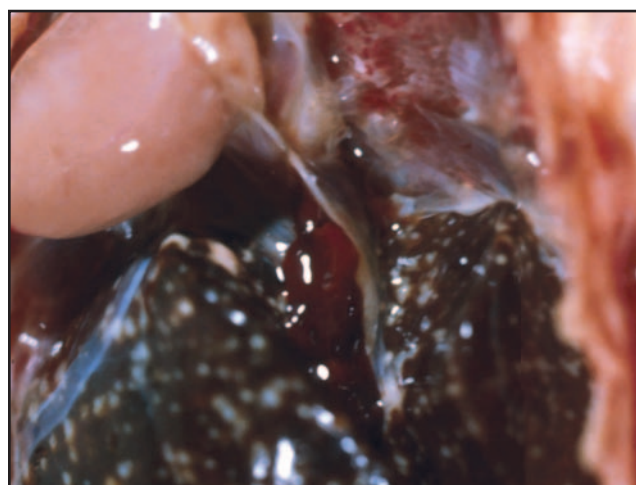
Fig 28.2 | Multifocal granulomatous lesions in the liver of a sandhill crane (*Grus canadensis*) caused by *Mycobacterium* spp.

in the gastrointestinal tract (Fig 28.1) and liver (paratuberculous) (Fig 28.2). Classic avian mycobacteriosis is associated with tubercles in many organs such as the kidney, liver and spleen, while diffuse disease may be associated with diffuse enlargement of affected organs.[24,29,80]

Granulomatous lesions are common in birds of prey but rare in pigeons and doves, waterfowl and most parrots (Table 28.2).[29] Diffuse mycobacteriosis has been most commonly reported in Coraciiformes, such as the kingfisher (*Alcedo* spp.), and Passeriformes.[32,61]

Granulomatous Intestinal Disease

Granulomatous intestinal or paratuberculous disease is associated with muscle wasting and emaciation. Initially the bird will display a good appetite, but anorexia later

develops. The presentation of wasting with an increased appetite can lead to the incorrect presumptive diagnosis of proventricular dilatation disease. Additional non-specific signs of illness might include poor feather quality, lethargy, weakness and pallor.[51] Chronic or intermittent diarrhea may also be observed.[12,29,80]

Abdominal distension due to enlargement of the liver or small intestines also might be detected. Ascites is rare, although it has been reported in Canada geese (*Branta canadensis*), mute swans (*Cygnus olor*), tundra swans (*Cygnus columbianus*) and some parrots.[86]

Musculoskeletal Disease

Reports in the literature describe anywhere from 2 to 93% incidence of bony lesions in avian mycobacteriosis.

Fig 28.3 | Granulomatous nodules within the skin of a lovebird (*Agapornis roseicollis*) caused by *Mycobacterium* spp.

Fig 28.4 | An irregular, firm, fleshy mass in the choana of a blue-fronted Amazon parrot (*Amazona aestiva*) caused by *Mycobacterium* spp.

Acute or chronic lameness, which might be shifting leg in nature, may be observed due to granulomatous lesions in bones or joints. The carpometacarpal and elbow joints are most commonly involved, and skin overlying the affected joints might be thickened and ulcerated.[29,80]

Respiratory Disease

Granulomas within the lungs or compression of air sacs secondary to hepatomegaly can lead to dyspnea or exercise intolerance. Additional signs of respiratory disease are rare with avian mycobacteriosis, although focal nodules have been reported within the infraorbital sinus, nares and syrinx.[14,71,85]

Skin Disease

Tubercle formation within the skin also is rare. Dermatitis, diffuse, non-pruritic thickening associated with xanthomatosis, as well as pale, soft, subcutaneous masses have been reported in association with avian mycobacteriosis **(Fig 28.3)**.[25,29,80]

Ocular Lesions

Granulomatous lesions may be associated with the eyelids, nictitating membranes, retrobulbar tissue and pecten.[1,62,71,77,85] There also is one report of keratitis associated with avian mycobacteriosis.[74]

Miscellaneous Lesions

In rare reports, granulomas have been found within the oropharynx **(Fig 28.4)**, larynx or external auditory canal.[1,29,85] Endocrine abnormalities such as reproductive failure might occur secondary to an infection in the adrenal glands, pancreas or gonads.[80] Avian mycobacteriosis also might be associated with neurologic signs due to involvement of the spinal cord, brain or vertebral column.[52,77,80]

ANTEMORTEM DIAGNOSTICS

Antemortem diagnosis of mycobacteriosis is difficult due to the wide variety of possible clinical signs and physical examination findings. A strong index of suspicion for avian mycobacteriosis can be based on signalment, clinical findings consistent with disease, profound leukocytosis, organomegaly and the cytologic presence of acid-fast bacteria. Serologic techniques such as enzyme-linked immunosorbent assay (ELISA) also may prove helpful in selected cases and are described in the following section on serology. A definitive diagnosis of mycobacteriosis relies on histologic identification or culture of the organism. Molecular techniques, such as DNA probes and nucleic acid amplification, also are promising in the aid of diagnosing avian mycobacteriosis.

Minimum Database

Minimum database results are variable. The complete blood count might reveal a marked heterophilic leukocytosis, monocytosis, thrombocytosis and elevated fibrinogen. Chemistry panel results often are unremarkable, although liver enzymes may be mildly to moderately elevated, and albumin levels may be decreased. Early in the disease process, a polyclonal gammaglobulinopathy also might be detected.[35,77,80]

Imaging

Radiographic findings can include hepatosplenomegaly and dilation of intestinal loops with gas **(Fig 28.5)**.[80] Gastrointestinal contrast radiography may demonstrate a thickened and irregular small intestinal wall. Granulomas may be identified within the bones, lungs or coelom, however, these lesions are more difficult to identify in the bird, since they do not calcify as in mammals.[77]

Radiographic findings involving bone might include lysis and/or sclerosis consistent with osteomyelitis, osteophy-

Fig 28.5 | Widening of the cardiohepatic silhouette on a V/D radiograph due to hepatomegaly caused by avian mycobacteriosis in an Amazon parrot (*Amazona* sp.).

tosis around arthritic joints, pathological fractures and endosteal bone densities.[77] Anatomic regions most commonly affected include the midshaft region of long bones, such as the humerus, tibiotarsus and ulna, and the ribs and sternum. There are rare reports of lesions involving the vertebrae and femur.[80] In an unusual case report, chondritis, osteitis and osteomyelitis were described in the nasal bone of a wood duck (*Aix sponsa*) with mycobacteriosis.[27]

Ultrasonography and alternate imaging methods, such as computed tomography, also are potentially useful diagnostic modalities.

Laparoscopy

Laparoscopy is an extremely useful technique for identifying lesions on the serosal surface of the liver, spleen, intestine, lung and air sacs. Granulomas may be visualized as white, yellow or tan round masses, which are soft and easily biopsied.[80]

Cytology

A large number of mycobacteria must be present (5 x 10^4/ml) before the organism can be visualized microscopically; therefore, fecal acid-fast stains serve as a poor screening tool. The Ziehl-Neelsen stain is the standard method for identification of acid-fast organisms. A modified Ziehl-Neelsen stain utilizes peanut oil to reduce damage to the mycobacterial cell wall. Mycobacteria appear pink-red with the Ziehl-Neelsen stain. *Mycobacterium tuberculosis* is rod-shaped, while *M. avium* can appear almost coccoid or as long, beaded rods.[3,77]

A suggestive diagnosis of avian mycobacteriosis may be based on identification of the organism in cytologic samples; however, the acid-fast stain is not a specific test, because non-pathogenic mycobacteria can be transient gastrointestinal inhabitants or environmental contaminants. Therefore, positive acid-fast cytology should be confirmed by culture, histopathology or DNA probe analysis.

Serology

Serologic tests available include hemagglutination (HA), complement fixation (CF) and ELISA. These tests are highly species-specific and they are available for only a limited number of species.

HA is a rapid, easy-to-perform assay run on whole blood or serum. The use of fresh whole blood might produce more sensitive (true positive) results than whole blood in EDTA or serum. Species-specific antigen is required for reliable results. HA has been of some use in waterfowl, domestic fowl, raptors and cranes.[21,35]

ELISA is a sensitive, albeit labor-intensive, test that requires at least 24 hours before results are available. Highly species-specific antigen is required. For instance, a sensitive and specific ELISA exists for mycobacteria in feral barnacle geese (*Branta leucopsis*).[16,19,21,28,77]

CF titers of 1:20 or greater have been used to confirm infection or exposure to *Mycobacterium avium* infection in grey-cheeked parakeets (*Brotogeris pyrrhopterus*).[58]

Culture

Culture has several practical limitations. *Mycobacterium* is only intermittently shed, and careful sample collection is necessary to prevent environmental contamination. Mycobacteria are difficult to culture, and no growth occurs even when proper protocols are followed. If growth does occur, at least 2 to 4 weeks are required for visible colonies to appear and up to 8 weeks of incubation is required. Some strains of *M. avium* require up to 6 months before colonies are identifiable.

Use of a radiometric culture method[a] reduces the length of time needed for culture. This acidic culture medium is especially useful for isolation of the fastidious *Mycobacterium genavense*. In one study, only 3 out of 34 *M. genavense* isolates grew on conventional solid media, while the acidic culture medium supported growth of 23/34 isolates.[41,43]

DNA Probes

The DNA probe assay is a rapid method for identifying various species of *Mycobacterium* grown in culture. Although a very sensitive (95%) and specific (100%) test,

the currently available gene probe[b] is not sensitive enough to directly detect acid-fast bacilli in specimens.[3]

Polymerase Chain Reaction

Molecular techniques may be used to identify organisms grown not only on culture media but also identified within fecal, biopsy or necropsy samples, including formalin-fixed paraffin-embedded sections.[4,34,47] Polymerase chain reaction (PCR) methods[c], based on the amplification and sequencing of the small subunit 16S rRNA gene of mycobacteria, have been used to identify *M. avium*, *M. bovis* and *M. genavense*.[9,47,56,60,76]

One study comparing the sensitivity and specificity of various samples found that fecal specimens had the highest sensitivity by PCR (77.8%). Processing fecal specimens with the zwitterionic detergent, C_{18}-carboxypropylbetaine (CB-18), also might increase the sensitivity of test results.[78]

Intradermal Skin Testing

Intradermal skin testing has been used for decades in poultry in the diagnosis of mycobacteriosis. A small volume (0.1 ml) of avian purified protein derivative tuberculin (PPD) is injected into the wattle or comb and assessed 48 to 72 hours later.[7,55,77]

Unfortunately, intradermal testing has proven unreliable in a number of avian species including pigeons, geese, quail and raptors. In these species, intradermal skin testing is frequently associated with false negatives, especially in the early and late stages of disease. Testing has been attempted on skin over the hock, vent, wing web and eyelid. The skin just behind the ear also has been utilized in ratites.[29,77]

POSTMORTEM DIAGNOSIS

Gross Findings

The gross necropsy findings of avian mycobacteriosis vary widely. Non-specific findings might include muscle wasting, loss of subcutaneous and intracoelomic fat and discolored, poor-quality feathers. There may be no significant gross findings in the diffuse form of mycobacteriosis.[59,80]

Organomegaly

Hepatosplenomegaly is one of the most consistent findings in songbirds and grey-cheeked parakeets (*Brotogeris* spp.) with mycobacteriosis.[11,63] Some birds may also demonstrate an enlarged, pale, firm liver due to amyloid deposition, which may eventually lead to hepatic rupture and hemorrhage.[77] Polycystic livers and cystic granulomas have been reported in waterfowl.[63]

Intestinal Lesions

Distension or thickening of the intestines is an extremely common finding in granulomatous intestinal disease. Intestinal mucosa also may display a "shaggy carpet" appearance caused by prominently thickened or clubbed villi.[77] Proventricular lesions also may be identified.[37]

Granulomas

Tubercles are frequently white, tan or yellow in color, and they might range in size from miliary foci to nodules several centimeters in diameter. Granulomas are most commonly located within the intestinal wall, liver, spleen and bone.[11,24,49,53,77] Granulomas also might be found in subcutaneous tissue as well as a variety of other viscera such as the kidney.[46] Tubercle formation within the skin and lungs is rare.[25,29]

Miscellaneous Lesions

Additional lesions that might be identified with avian mycobacteriosis include the following: proliferative or lytic bony lesions (secondary pathologic fractures are possible),[77] dermatitis or diffuse thickening of the skin associated with xanthomatosis,[80] and pulmonary necrosis or ulceration.[24,53] A single fluid-filled pulmonary cyst has been reported in a cockatoo.[57] An extremely unusual manifestation of mycobacteriosis was reported in fairy bluebirds (*Irena* spp.) with granulomatous cardiopulmonary arteritis.[50]

Histologic Findings

The most common findings reported include granulomatous enteritis, splenitis or hepatitis with variable amounts of acid-fast bacteria. A marked accumulation of macrophages also may be identified within the dermis, mucous membranes and subserosa of the peritoneum and airsacs.[24] Granulomatous intestinal lesions can also be associated with expansion of the intestinal villi by diffuse granulomatous infiltrate and proliferations of epithelial cells within the glands of Lieberkuhn.[29,83]

Large numbers of acid-fast rods are found in lesions caused by *Mycobacterium avium*, while *M. bovis* and *M. tuberculosis* tend to be found in relatively small numbers.[80]

Granulomas generally do not possess a region of central calcification or an extensive necrotic center.[80] The necrotic regions that are identified in avian mycobacterial granulomas are surrounded by epithelioid cells, multinucleated giant cells and lymphocytes.[38,53] Non-caseous granulomas may contain large macrophages with highly vacuolated cytoplasm and numerous acid-fast bacteria.[60]

The diffuse form of avian mycobacteriosis is more difficult to recognize at necropsy, because organomegaly may not be observed. Instead, a diffuse infiltration with

Table 28.3 | Anti-mycobacterial Drugs[5,8,66,81,82]

- Aminoglycosides -
  Amikacin, Aminosidine,
  Kanamycin, Streptomycin
- Clofazimine
- Cycloserine
- Dapsone
- Ethambutol
- Ethionamide
- Fluoroquinolones -
  Ciprofloxacin,
  Enrofloxacin
- Isoniazid
- Macrolides -
  Azithromycin,
  Clarithromycin
- Pyrazinamide
- Rifamycins -
  Rifabutin, Rifampin
- Tetracyclines -
  Doxycycline

large, foamy histiocytes may be seen.[23,32,61]

THERAPEUTICS

Humane euthanasia is recommended for birds diagnosed with mycobacteriosis. Birds infected with *Mycobacterium avium* may continuously shed large numbers of organisms into the environment.[77,81] This potential zoonotic risk is especially important in households with immunosuppressed individuals, such as those on chemotherapy, the very young, the elderly and human immunodeficiency virus (HIV)-positive. Any humans in contact with an infected bird should consult a physician for evaluation.

Surgery

Surgical excision may be possible and perhaps even curative for discrete nodules in the skin, subcutaneous tissue or periocular tissue. Medical management is indicated for disseminated avian mycobacteriosis when treatment is deemed appropriate.

Medical Management

There are numerous drugs with anti-mycobacterial activity **(Table 28.3)**. *Mycobacterium avium* isolated from human patients has been reported sensitive to azithromycin, clarithromycin, ciprofloxacin, rifabutin, rifampicin, amikacin, clofazimine and ethambutol. Doxycycline has shown efficacy against atypical mycobacterium like *M. fortuitum*.[81]

Multi-drug therapy should be employed in the treatment of avian mycobacteriosis. Numerous successful combinations have been reported in the literature **(Table 28.4)**.[8,65,66,75,81,82] Due to the intracellular nature of the pathogen, its slow growth, and the bacteriostatic activity of most anti-mycobacterial drugs, an extended course of treatment lasting 4 months or longer is recommended.

Immunotherapy has been a useful adjunct for treatment of human tuberculosis patients.[72,73] Administration of killed *M. vaccae* has some immunomodulatory effects and has been associated with an improvement in sur-

Table 28.4 | Multi-Drug Therapy[5,8,66,81,82]

Drug	Therapy
Rifabutin-Ethambutol-Clarithromycin	
Rifabutin	15 mg/kg PO q 24 h
Ethambutol	30 mg/kg PO q 24 h
Clarithromycin	85 mg/kg PO q 24 h (allometrically scaled)
Rifabutin-Ethambutol-Azithromycin*	
Rifabutin	15 mg/kg PO q 24 h
Ethambutol	30 mg/kg PO q 24 h
Azithromycin **or**	43 mg/kg PO q 24 h
Rifabutin	56 mg/kg PO q 24 h
Ethambutol	56-85 mg/kg PO q 24 h
Azithromycin **or** Clarithromycin	43 mg/kg PO q 24 h **or** 85 mg/kg PO q 24 h
Rifampin-Ethambutol-Clofazimine	
Rifampin	45 mg/kg PO q 24 h
Ethambutol	30 mg/kg PO q 24 h
Clofazimine	6 mg/kg PO q 24 h
Rifampin-Ethambutol-Isoniazid**	
Rifampin	45 mg/kg PO q 24 h
Ethambutol	30 mg/kg PO q 24 h
Isoniazid	30 mg/kg PO q 24 h
Rifampin-Ethambutol-Streptomycin	
Rifampin	15 mg/kg PO q 12 h
Ethambutol	10 mg/kg PO q 12 h
Streptomycin	30 mg/kg IM q 12 h
Rifabutin-Ethambutol-Enrofloxacin	
Rifabutin	15 mg/kg PO q 24 h
Ethambutol	30 mg/kg PO q 24 h
Enrofloxacin	30 mg/kg PO q 24 h
Rifabutin-Ethambutol-Ciprofloxacin	
Rifabutin	15 mg/kg PO q 24 h
Ethambutol	30 mg/kg PO q 24 h
Ciprofloxacin	80 mg/kg PO q 24 h
Ethambutol-Cycloserine-Clofazimine-Enrofloxacin (raptors)	
Ethambutol	20 mg/kg PO q 12 h
Cycloserine	5 mg/kg PO q 12 h
Clofazimine	1.5 mg/kg PO q 24 h
Enrofloxacin	10-15 mg/kg PO, IM q 12 h
Lamprene-Seromycin-Myambutol	
Lamprene	1.5 mg/kg PO q 24 h
Seromycin	10 mg/kg PO q 12 h
Myambutol	40 mg/kg PO q 12 h
With advanced cases give	
Ciprofloxacin **or**	20 mg/kg PO q 12 h
Enrofloxacin **or**	15 mg/kg PO q 12 h
Streptomycin	20-40 mg/kg IM q 12 h x 7-10d

*Lower doses have been reported
**Drugs are mixed into a dextrose powder, then mixed into a small amount of food and given PO q 24 h.

vival rates. *Mycobacterium vaccae* was used in a small trial in captive waterfowl; however, results were inconclusive.[11]

CONTROL AND PREVENTION

Mycobacterium is extremely stable in the environment. It is highly resistant to environmental extremes and might

survive for months or years in contaminated soil and surface water or less commonly in feed, feathers or discarded food.[24]

There are no absolute means for control of avian tuberculosis. Quarantine and surveillance programs must strive to identify and eliminate infected animals. Providing complete, balanced nutrition and utilizing good sanitation practices will minimize the impact of disease. Stressors such as overcrowding also must be minimized.[26]

Identification and Elimination of Infected Animals

The poultry industry has relied on the use of intradermal skin testing to identify and then eradicate affected birds. Unfortunately, this screening test has not proven useful in the exotic avian species studied to date.[30,40,51,77] In a zoological or aviary setting, an extended quarantine period of 3 to 6 months should be considered.[40,43] During this time, screening tests should include physical examination, hematology, serum biochemistry, acid-fast fecal smears and serology in those species for which it is available. Laparoscopy, fecal culture and PCR testing also should be considered.

If birds with confirmed mycobacteriosis are not euthanized, they must be kept permanently separated from other birds. Birds that were in contact with mycobacteria-positive individuals also should be quarantined for 1 to 2 years. During this time, periodic retesting every 6 to 12 weeks for mycobacteriosis is recommended.[26,77]

Removal or Prevention of Tuberculosis in the Environment

To reduce the risk of exposure to mycobacteria, carefully consider cage design and sanitation. Prevent contact with wild birds. In aviaries or zoological collections, one should consider solid, non-porous flooring and other easily disinfected surfaces instead of dirt substrate. Footbaths should be utilized to minimize the potential introduction of mycobacteria into the enclosure.[23,43]

Tuberculosis is more resistant to disinfectants than other non-spore-forming bacteria.[77] Compounds with antimy-

cobacterial activity include alcohol, aldehydes, halogens, peroxygens and phenols **(Table 28.5)**.[67] The use of reed biofiltration systems to remove contamination from water also is being investigated.[77]

Vaccination

There are only rare reports of vaccination against mycobacteriosis in birds. The bacille Calmette-Guérin (BCG) vaccine, a human product directed against *Mycobacterium tuberculosis*, was tried in poultry but was found to be of little benefit.[33] A vaccine against *Mycobacterium avium* also has been given to poultry and, more recently, captive waterfowl in Britain.[54,64]

ZOONOTIC POTENTIAL OF AVIAN MYCOBACTERIOSIS

Are birds that live in close proximity to people a potential source of tuberculosis? Although the incidence of *M. avium* infection in human acquired immunodeficiency syndrome (AIDS) patients is increasing,[40] these mycobacterial strains are thought to be environmental in origin. Studies using DNA probes have shown that avian strains of *M. avium* rarely infect people.[2] Birds and humans are probably exposed to the same environmental sources of mycobacteria.[31]

CONCLUSION

Avian mycobacteriosis may be caused by MAI or atypical mycobacteria such as *M. genavense*. Birds usually are exposed to mycobacteria through soil or water contaminated by feces. Clinical disease varies with the species and strain of *Mycobacterium* spp., the species of bird affected and the route of transmission. Classically, however, mycobacteriosis is a disease of the gastrointestinal tract and liver in the bird. While identification of disease relies on intradermal skin testing in poultry, this has not proved useful in other avian species. Ancillary testing in nongallinaceous birds should include a complete blood count, imaging, laparoscopy, cytology, serology and PCR testing. A definitive diagnosis is based on culture or histopathology. Euthanasia is recommended for affected birds. Control should focus on identification of affected birds through quarantine and use of appropriate screening tests. Avoiding dirt flooring may reduce exposure to infectious material. Instead, utilize non-porous, easy-to-clean surfaces, appropriate disinfectants and footbaths.

Table 28.5 | Anti-mycobacterial Compounds[5,8,66,81,82]

- Alcohol
- Aldehydes -
   Formaldehyde,
   Glutaraldehyde,
   Succinaldehyde, Glyoxal
- Halogens -
   Chlorine-releasing
   agents, Iodine-releasing
   agents
- Peroxygens
- Phenolics
- Chemosterilizing gases -
   Ethylene oxide, Beta-
   propiolactone

Products Mentioned in the Text

a. BACTEC System, Becton Dickinson, Diagnostic Instrument Systems, Inc, Sparks, MD, USA, www.bd.com/clinical/products/mycob

b. AccuProbe System, GenProbe Inc, San Diego, CA, USA, www.gen-probe.com/prod_serv/mycobac_accuprobe.asp

c. Roche Molecular Systems, Branchburg, NJ, USA, www.roche-diagnostics.com/ba_rmd/products.html

References and Suggested Reading

1. Ackerman LJ, Benbrook SC, Walton BC: *Mycobacterium tuberculosis* infection in a parrot. Am Rev Resp Dis 109(3):388-390, 1974.

2. Angulo FJ, et al: Caring for pets of immunocompromised persons. J Am Vet Med Assoc 205(12):1711-1718, 1994.

3. Aranaz A, et al: Laboratory diagnosis of avian mycobacteriosis. Sem Avian & Exotic Pet Med 6(1):9-17, 1997.

4. Bascunana CR, Belak K: Detection and identification of mycobacteria in formalin-fixed, paraffin-embedded tissues by nested PCR and restriction enzyme analysis. J Clin Microbiol 34(10):2351-2355, 1996.

5. Bauck L, Hoefer HL: Avian antimicrobial therapy. Sem Avian & Exotic Pet Med 2:17-22, 1993.

6. Behlert O, Gerlach H: Control of avian mycobacterial infection in the pheasantry at Cologne zoo. Berliner and Munchener Tierarztliche Wochenschrift 104(1):12-15, 1991.

7. Bernardelli A, et al: Mycobacterial infections in sea mammals and birds. Revue Scientifique et Technique 9(4):1121-1129, 1990.

8. Beynon PH, Forbes NA, Harcourt-Brown NH (eds): BSAVA Manual of Raptors, Pigeons and Waterfowl. Ames, IA, Iowa State University Press, 1996.

9. Boian M, et al: Identification of *Mycobacterium genavense* in intestinal tissue from a parakeet using two polymerase chain reaction methods: Are pets a reservoir of infection in AIDS patients? AIDS 11(2):255-256, 1997.

10. Böttger EC, et al: Disseminated "*Mycobacterium genavense*" infection in patients with AIDS. Lancet 340(8811):76-80, 1992.

11. Brown MJ, Cromie RL: Weight loss and enteritis. *In* Beynon PH, Forbes NA, Harcourt-Brown NH (eds): BSAVA Manual of Raptors, Pigeons and Waterfowl. Iowa State University Press, Ames, Iowa, 1996, pp 322-329.

12. Butcher GD, et al: Mycobacterium infection in a gray-cheeked parakeet. Avian Dis 34(4):1023-1026, 1990.

13. Butler KL, et al: Experimental inoculation of European starlings and American crows with *Mycobacterium bovis*. Avian Dis 45(3):709-718, 2001.

14. Campbell T: Mycobacterial tracheitis in a double-yellow headed Amazon parrot (*Amazona ochrocephala oratrix*). Exotic Pet Practice 2(1):7, 1997.

15. Clark SL, Collins MT: A single dose oral challenge model of disseminated *Mycobacterium avium* infection. Abstracts General Meeting American Society for Microbiology, 1995, p 139.

16. Clark SL, Collins MT, Price JI: New methods for diagnosis of *Mycobacterium avium* infection in birds. Proc Am Assoc Zoo Vet and Am Assoc Wildl Vet, 1995, pp 151-154.

17. Clippinger TL, Bennet RA, Newell SA: Radiographic diagnosis-Granulomatous pneumonia with intralesional acid-fast bacilli in an Amazon parrot. Vet Radiol Ultrasound 39(3):181-184, 1998.

18. Converse KA, Dein FJ: Tuberculosis in wild birds: Implications for captive birds. Proc Am Assoc Zoo Vet, 1990, p 140.

19. Coyle MB, et al: Laboratory aspects of "*Mycobacterium genavense*," a proposed species isolated from AIDS patients. J Clin Microbiol 30(12):3206-3212, 1992.

20. Cromie RL, et al: Avian immune responses to *Mycobacterium avium*: The wildfowl example. Dev Comp Immunol 24(2-3):169-185, 2000.

21. Cromie RL, et al: A comparison and evaluation of techniques for diagnosis of avian tuberculosis in wildfowl. Avian Pathol 22:617-630, 1993.

22. Cromie RL, et al: Susceptibility of captive wildfowl to avian tuberculosis: The importance of genetic and environmental factors. Tubercle 72(2):105-109, 1991.

23. Derrickson SR, Pickett C: History of avian tuberculosis at the national zoological park: Gaining control through management and husbandry. Proc Am Assoc Zool Parks and Aquariums, 1991, pp 476-484.

24. Dorrestein GM: Bacteriology. *In* Altman RB, et al (eds): Avian Medicine and Surgery. Philadelphia, PA, WB Saunders Co, 1997, pp 275-280.

25. Drew ML, Ramsay E: Dermatitis associated with *Mycobacterium* spp. in a blue-fronted Amazon parrot. Proc Assoc Avian Vet, 1991, pp 252-254.

26. Ensley PK, et al: Avian tuberculosis at the National Zoological Park. Proc Am Assoc Zoo Vet, 1975, pp 203-206.

27. Ferguson SH, et al: *Mycobacterium intracellulare* (*Battey bacillus*) infection in a Florida wood duck (*Aix sponsa*). Am Rev Respir Dis 100:876-879, 1969.

28. Forbes NA, et al: Diagnosis of avian tuberculosis in waterfowl. Proc Assoc Avian Vet, 1993, pp 182-186.

29. Gerlach H: Bacteria. *In* Ritchie B, Harrison G, Harrison L (eds): Avian Medicine: Principles and Applications. Brentwood, TN, HBD Intl, 1999, pp 949-983.

30. Gill IJ, Blandy ML: Control of avian tuberculosis in a commercial poultry flock. Aust Vet J 63(12):422-423, 1986.

31. Grange JM, Yates MD, Broughton E: A review: The avian tubercle bacillus and its relatives. J Appl Bacteriol 68(5):411-431, 1990.

32. Griner LA: Atypical tissue reaction to *M. avium* in Passeriformes and Coraciiformes. *In* Montali R (ed): Mycobacterial Infection of Zoo Animals. Washington DC, Smithsonian Institution Press, 1976, pp 205-207.

33. Guindi SM: Vaccination of fowls against tuberculosis: An experimental study on the immunizing value of BCG vaccine, and a heat-killed tubercle bacilli vaccine (avian type). Proc 1ˢᵗ Annual Veterinary Conference, 1960, pp 93-104.

34. Gyimesi Z, et al: Detection of *Mycobacterium avium* subspecies avium in formalin-fixed, paraffin-embedded tissues of captive exotic birds using polymerase chain reaction. J Zoo Wildl Med 30(3):348-353, 1999.

35. Hawkey C, et al: Hematological changes in domestic fowl (*Gallus gallus*) and cranes (Gruiformes) with *Mycobacterium avium* infection. Avian Pathol 19:223-234, 1990.

36. Hines ME, Kreeger JM, Herron AJ: Mycobacterial infections of animals: Pathology and pathogenesis. Lab Anim Sci 45(4):334-351, 1995.

37. Hoefer HL: Gastric disorders in pet birds. Proc Mid-Atlantic States Assoc Avian Vet, 1997, pp 106-110.

38. Holsboer-Buogo C, et al: Presence of *Mycobacterium genavense* in birds. Schweizer Archiv für Tierheilkunde 139(9):397-402, 1997.

39. Hoop RK: *Mycobacterium tuberculosis* infection in a canary (*Serinus canana* L.) and a blue-fronted Amazon parrot (*Amazona amazona aestiva*). Avian Dis 46(2):502-504, 2002.

40. Hoop RK: Public health implications of exotic pet mycobacteriosis. Sem Avian & Exotic Pet Med 6(1):3-8, 1997.

41. Hoop RK, Böttger EC, Pfyffer GE: Etiologic agents of mycobacteriosis in pet birds between 1986 and 1995. J Clin Microbiol 34(4):991-992, 1996.

42. Hoop RK, et al: Mycobacteriosis due to *Mycobacterium genavense* in six pet birds. J Clin Microbiol 31(4):990-993, 1993.

43. Isaza R: Tuberculosis in all taxa. *In* Fowler ME, Miller RE (eds): Zoo and Wild Animal Medicine, 5ᵗʰ ed. Philadelphia, PA, WB Saunders Co, 2003, pp 89-696.

44. Jahans KL: The isolation of an atypical mycobacterium from three wood pigeons with tuberculosis-like lesions. Res Vet Sci 24(3):378-379, 1978.

45. Kock ND, et al: *Mycobacterium avium*-related epizootic in free-ranging lesser flamingos in Kenya. J Wildl Dis 35(2):297-300, 1999.

46. Marco I, Domingo M, Lavin S: *Mycobacterium* infection in a captive-reared capercaillie. Avian Dis 44(1):227-230, 2000.

47. Miller JM, Jenny AL, Ellingson JL: Polymerase chain reaction identification of *Mycobacterium avium* in formalin-fixed, paraffin-embedded animal tissues. J Vet Diagn Invest 11(5):436-440, 1999.

48. Montali RJ, Mikota SK, Cheng LI: *Mycobacterium tuberculosis* in zoo and wildlife species. Rev Sci Tech Int Epiz 20(1):291-303, 2001.

49. Morita Y, et al: Pathogenicity of *Mycobacterium avium* complex serovar 9 isolated from painted quail. J Vet Med Science 61(12):1309-1312, 1999.

50. Morton LD, et al: Granulomatous aortitis and cardiopulmonary arteritis in fairy-bluebirds (*Irena puella*) with mycobacteriosis. Proc Am Assoc Zoo Vet, 1997, pp 272-273.

51. Mutalib AA, Riddell C: Epizootiology and pathology of avian tuberculosis in chickens in Saskatchewan. Can Vet J 29:840-842, 1988.

52. Odiawo GO, Mukurira JM: Avian cerebral tuberculosis. Vet Rec 122(12):279-280, 1988.

53. Ozcan K, et al: Tuberculosis in geese in Turkey. Avian Dis 45(3):755-759, 2001.

54. Painter KS: Avian tuberculosis caused by *Mycobacterium avium* serotype 3 in captive wildfowl. Vet Rec 140(17):457-458, 1997.

55. Pavlas M, Patlokova V: Occurrence of mycobacteria in sawdust, straw, hay and their epizootiological significance. Acta Veterinaria Brno 54(1):85-90, 1985.

56. Pavlik I, et al: Relationship between IS901 in the *Mycobacterium avium* complex strains isolated from birds, animals, humans, and the environment and virulence for poultry. Clin Diag Lab Immunol 7(2):212-217, 2000.

57. Peavy GM, Silverman S, Howard EB: Pulmonary tuberculosis in a sulfur-crested cockatoo. J Am Vet Med Assoc 169(9):915-919, 1976.

58. Phalen DN, et al: Serologic diagnosis of mycobacterial infections in birds (a preliminary report). Proc Assoc Avian Vet, 1995, pp 67-73.

59. Portaels F, et al: Mycobacteriosis caused by *Mycobacterium genavense* in birds kept in a zoo-11-year survey. J Clin Micro 34(2):319-323, 1996.

60. Ramis A, et al: *Mycobacterium genavense* infection in canaries. Avian Dis 40(1):246-251, 1996.

61. Reed R, et al: Clinical challenge. J Zoo Wildl Med 23(3):383-386, 1992.

62. Rich G: Avian mycobacterial infection. Exotic Pet Prac 5(6):47, 2000.

63. Roffe TJ: Isolation of *Mycobacterium avium* from waterfowl with polycystic livers. Avian Dis 33(1):195-198, 1989.

64. Rossi I: Immunizing potency of inactivated and living *Mycobacterium avium* and *Mycobacterium intracellulare* vaccines against tuberculosis of domestic fowls. Acta Vet 43:133-138, 1974.

65. Rosskopf WJ, Woerpel RW: Avian diagnosis: Laboratory interpretations and case reports, Part 3. Comp Anim Pract 19(1):41-48, 1989.

66. Rupley AE: Respiratory, bacterial, fungal and parasitic diseases. Proc Small Mam and Rept Med Surg, Assoc Avian Vet, 1997, pp 23-44.

67. Russell AD: Activity of biocides against mycobacteria. Soc Appl Bacteriol Symp Ser 25:875-1015, 1996.

68. Sato Y, et al: An occurrence of avian tuberculosis in hooded merganser (*Lophodytes cucullatus*). Avian Dis 40(4):941-944, 1996.

69. Sijben JWC, et al: Dietary linoleic acid divergently affects immune responsiveness of growing layer hens. Poul Sci 79(8):1106-1115, 2000.

70. Silva-Krott I, Brock MK, Junge RE: Determination of the presence of *Mycobacterium avium* on Guam as a precursor to reintroduction of indigenous bird species. Pac Conserv Biol 4:227-231, 1998.

71. Smits B: Non-viral diseases of

psittacines. Surveillance 24(2):17-18, 1997.

72. Stanford JL: Immunotherapy with *Mycobacterium vaccae* in the treatment of mycobacterial disease. J Infect 39(3):179-82, 1999.

73. Stanford JL, Stanford CA: Immunotherapy with *Mycobacterium vaccae* and the treatment of tuberculosis. Soc Appl Bacteriol Symp Ser 25:81S-86S, 1996.

74. Stanz KM, Miller PE, Cooley AJ: Mycobacterial keratitis in a parrot. J Am Vet Med Assoc 206(8):1177-1180, 1995.

75. Stauber EH: Treatment of psittacine pet birds with avian mycobacteriosis-case reports (Behandlung der aviären mykobakteriose bei papageienartigen stubenvögeln -Fall Berichte). VIII. Tagung der Fachgruppe "Geflugel-

krankheiten", 1992, pp 231-238.

76. Telenti A, et al: Rapid identification of mycobacteria to the species level by polymerase chain reaction and restriction enzyme analysis. J Clin Microbiol 31(2):175-178, 1993.

77. Tell LA, Woods L, Cromie RL: Mycobacteriosis in birds. Rev Sci Tech Int Epiz 20(1):180-203, 2002.

78. Thornton CG, et al: Processing postmortem specimens with C_{18}-carboxypropylbetaine and analysis by PCR to develop an ante-mortem test for *Mycobacterium avium* infection in ducks. J Zoo Wildl Med 30(1):11-24, 1999.

79. Tuzova RV: Antigenic activity of bovine and avian type *Mycobacterium* in hens. Trudy-Belorusskii-Nauchno-Issledovatel'skii-Veterinarnyi-

Institut 13:30-33, 1975.

80. Van der Heyden N: Clinical manifestations of mycobacteriosis in pet birds. Sem Avian & Exotic Pet Med 6(1):18-24, 1997.

81. Van der Heyden N: New strategies in the treatment of avian mycobacteriosis. Sem Avian & Exotic Pet Med 6(1):25-33, 1997.

82. Van der Heyden N: Update on avian mycobacteriosis, Proc Assoc Avian Vet, 1994, pp 53-61.

83. Van der Schaaf A, Hopmans JLH, Van Beek J: Mycobacterial intestinal disease in wood pigeons (*Columba palumbus*). Tijdschr Diergeneeskd 101(19):1084-1092, 1976.

84. Wald A, et al: Infection with fastidious mycobacterium resembling *Mycobacterium simiae* in seven patients with AIDS. Ann Intern Med 117(7):586-589, 1992.

85. Washko RM, et al: *Mycobacterium tuberculosis* infection in a green-winged macaw (*Ara chloroptera*): report with public health implications. Clin Microbiol 36(4):1101-1102, 1998.

86. Wobeser GA: Other bacteria, mycoplasmas and chlamydiae. *In* Wobeser GA (ed): Diseases of Wild Waterfowl. New York, Plenum Press, 1997, pp 73-74.

87. Woerpel RW, Rosskopf W: Retro-orbital *Mycobacterium tuberculosis* infection in a yellow-naped Amazon parrot (*Amazona ochrocephala auropalliata*). Proc Assoc Avian Vet, 1983, pp 71-76.

88. Zorawski C, Skwarek P: Properties of *Mycobacterium avium* and atypical mycobacteria isolated from animals in Poland. Medycyna-Weterynaryjna 32(11): 661-664, 1976.